UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,561	03/01/2007	Howard J. Federoff	29556.1692 (6-1275)	7894

11951 7590 01/09/2012

LeClairRyan
70 Linden Oaks
Suite 210
Rochester, NY 14625

EXAMINER	
KELLY, ROBERT M	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
01/09/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,561	FEDEROFF ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *28-31,33,34,49 and 51* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *28-31,33,34,49 and 51* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment of 11/18/11 and argument of 8/23/11 are entered.

Claim 28 is amended.

Claim 50 is cancelled.

Claims 28-31, 33, 34, 49, and 51 remain pending.

Claim Status, Cancelled Claim(s)

In light of the cancellation of Claim 50, all rejections and/or objections to such claim(s) are rendered moot, and thus, are withdrawn.

Specification

In light of the amendment to the specification, the objection to such for new matter is withdrawn.

To wit, applicant has now listed the proper citation of what were considered the essential genes, and incorporation of the method is clearly in the other citation which was originally provided for such information.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejecitons of Claims 28-31, 33, 34, 49, and 51 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn.

To wit, the amendment follows the examiner's suggestions and provides all the genes properly as cited in the prior art utilized to provide such essential HSV genes.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 28-31, 33, 34, 49 and 51 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter, are withdrawn.

To wit, the amendment to the specification now properly cites the genes considered essential in the cited prior art for such possession.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 28-31, 33, 34 and 49 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, are withdrawn.

To wit, the amendment now only cites the single disclosed accessory protein, the VHS protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-31, 33, 34, and 49 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,946,135 to Schenk; Stavropoulos, et al. (1998) Journal of Virology, 72(9):7137-43; Saeki, et al. (1998) Human Gene Therapy, 9: 2787-94, and as further evidenced by Town, et al. (2002) Journal of Neuroimmunology, 132: 49-59, remain rejected, for reasons of record.

It should be noted that the rejection remains the same, except that the various components of the product-by-process of the claims rejected ("produced by a helper virus-free method comprising ....") are only interpreted on their basis as being a product-by-process, and not required of the claim. Specifically, there is nothing in the claim requiring the steps to be performed, but simply that the product administered is equivalent to one produced by the method of product-by-process listed in the claim.

Schenk '855 claims methods of treating diseases with Abeta deposits, including Alzheimer's disease, by administration of Abeta to thereby raise antibodies and treating the disease by the antibodies raised (Claims). Schenk '127 claims similar treatments, and teaches in the specification that the peptide may be alternatively delivered via a viral vaccine, wherein the protein is encoded in a vector, which is expressed by the cells, and in one embodiment HSV may be used as the vector, which should be non-pathogenic or attenuated (e.g., Section entitled "III. Therapeutic Agents", subsection entitled "1. Alzheimer's Disease", paragraph 9). Schenk '135 Claims treatment of the same with Abeta linked to a carrier molecule, and teaches in the specification that Keyhole limpet hemocyanin and tetanus toxoid may be used (Section entitled "III. Therapeutic Agents", subsection "1. Alzheimer's Disease", subsection entitled "3. Carrier Proteins").

Stavropoulos and Saeki both discuss the growth of amplicons in the absence of helper virus. Stavropoulos discusses the second-generation packaging system for HSV amplicons, which is centered on the use of five overlapping HSV-1 cosmid clones that together encode the wild-type viral genome but lack the required sequences for cleavage and packaging (p. 7138, col. 1, paragraph 2). Stavropoulos then modified the system by providing a single BAC with all the elements required for replication and packaging of the amplicon, but lacking the viral sequences for cleavage and packaging (e.g., p. 7140, col. 2, paragraph 2-p. 7141, col. 1, paragraph 2). Saeki teaches similar prior art knowledge with regard to the five overlapping HSV-1 cosmid clones for production of helper-free virus amplicons (e.g., p. 2788, paragraph bridging columns) and similar production of a single bacterial artificial chromosome for production of helper-free viral amplicons (p. 2788, col. 2, paragraph 2). Still further, both Stavropoulos and Saeki teach

that the amplicons contain nucleic acid sequences encoding an accessory protein for replication in E. coli (e.g., Saeki, p. 2787, paragraph bridging columns, reciting the use of antibiotic resistance gene for amplicillin).

With regard to inducing a Th2 mediated immune response, Abeta has been shown by Town to so-induce such a response (e.g., Title), and, absent reason to believe otherwise, the desired effect is there, because any absence of comment does not mean the structure is the same.

With regard to the presence of a nucleic acid encoding VHS, at least Saeki has nothing that indicates that such gene has been removed, and hence, absent reason to believe otherwise, the nucleic acid may be present in the helper-free virus systems.

Lastly, one may question whether a nucleic acid could provide protein for inducing immune response to the Abeta protein. However, as is shown in Herrlinger, vaccination therapy works, and hence, protein is produced in high enough levels to have an affect (whole article, and discussing previous findings (p.1436).

Hence, it would have been obvious to modify the HSV vectors of Schenk to deliver a gene encoding Abeta and a gene encoding keyhole limpet hemocyanin, and grow such in a helper-free virus method like that of Stavropoulos and Saeki, to then administer the helper-free viral amplicon to treat Alzheimer's disease. The Artisan would do so to treat the disease. Moreover, the Artisan would have a reasonable expectation of success, as Schenk teaches it will work, and claims similar protein therapy, Stavropoulos and Saeki teach the method of amplicon manufacture, and Herrlinger demonstrates the biologically-relevant levels of protein being produced.

Response to Argument - 103, Schenk (3), Stravopoulos, and Saeki (as by Towne)

Applicant's response of 8/23/11 has been fully considered but is not found persuasive.

Applicant argues that neither Sravropoulos nor Saeki teach the product-by-process claimed (pp. 8-9, paragraph bridging).

Such is not persuasive. The claim does not require the steps be performed either, but that a composition, which can be produced by the method of the product-by-process, is administered. The structure herein is the same, and as such, the argument made by Applicant is flawed. Specifically, arguments to the shutoff protein being the accessory protein is flawed, because the administered composition is the same in either case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-31, 33, 34, 49 and 51 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,946,135 to Schenk; Stavropoulos, et al. (1998) Journal of Virology, 72(9):7137-43; Saeki, et al. (1998) Human Gene Therapy, 9: 2787-94, and as further evidenced by Town, et al. (2002) Journal of Neuroimmunology, 132: 49-59 as applied to claims 28-31, 33, 34, 49, and 50 above, and further in view of Whitley, et al. (1998) Clinical Infectious Diseases, 26: 541-53, for reasons of record.

This rejection is made to overcome possible arguments that VHS is actually deleted in the vector systems of Saeki.

While the art in the base rejection appears to make obvious the invention, there is no specific teaching that VHS is actually included in the Saeki vectors, and hence, where above, the Examiner has relied upon the inherent nature to state that absent reason to believe otherwise, here, the Examiner provides the knowledge that VHS may be used in such vector systems.

Whitley teaches VHS (A.K.A.: UL41) degrades all mRNA, but that because viral transcription occurs at a very high rate, viral protein synthesis is less affected than host cell protein synthesis (p. 543, col. 1, point 2).

Hence, the Artisan would be further motivated to include the VHS encoding sequence into the chromosome, or add it separately through another plasmid. The Artisan would do so to shut down host protein synthesis preferentially, and thereby increase the relative production of proteins for amplicon manufacture and packaging. Moreover, the Artisan would have a reasonable expectation of success, as Whitley teaches the known functional consequences of the VHS protein, and there is nothing to question the efficacy of the method.

Lastly, with regard to the provision of providing a cell expressing VHS protein, such is simply a design choice. The VHS may be provided as a vector separately transfected into the cell, but all that is required is the expression of VHS to affect the method, and as such, it may be integrated into the genome, or simply provided in another vector, prior to the other transfections, and still, the effect is logically the same. Hence, because it is utilized for an art-recognized purpose, it is reasonably predictable to effect production of HSV particles in the method. Therefore, it is also obvious.

Response to Argument – Further in view of Whitley

Applicant's argument of 8/23/11 has been fully considered but is not found persuasive.

Applicant argues that combining Whitley, Schenk 855, Schenk 127, Schenk 135, Stravropoulous, Saeki, and Town is improper, because Whitley is non-analogous Art, and as such, there is no motivation to consider Whitley at the time of invention. Specifically, Applicant argues that the test is two-part, citing several pieces of case law. The test requires an inquiry as to (i) whether the art is from the same problem solving field of endeavor, and (ii) if it is not from the same field of endeavor, if it is still reasonably pertinent to the particular problem with which the inventor is involved. Applicant argues, with this test, that Whitely is a review article of HSV structure and replication, infection and clinical manifestation, and strategies for the prevention and treatment of HSV infection. Further, it is stated that Whitely teaches vhs plays a role in natural viral infection by inducing an RNA activity which degrades all mRNA. Next, it is argued that the problem solving area of the present invention is treating a patient having neurodegenerative disease with HSV amplicons produced from helper-virus free systems, and as such, Whitely is not at all pertinent to the invention as claimed (pp. 9-10).

Such is not persuasive. It is very clear that the claims are to treating neurodegenerative diseases characterized by plaque formation, with an HSV vector encoding a protein. Whitely teaches HSV viruses. To argue that the Artisan interested in utilizing HSV as a vector would not make himself/herself fully aware of the functions of the proteins and structure of HSV, seems ridiculous to the Examiner. The Artisan would definately make sure he/she understood the virus and how to make it, and to do so in the safest way possible, to perform the methods of use under controlled conditions. Just like Applicant must enable and possess a method of making and

using, the Artisan is not just interested in the composition, but must understand its components, as any Artisan would in this field of biology. Hence, it is beyond the examiner's ability to even consider this art to be art that the Artisan would not be aware of. Lastly, it should be noted for the record, that Whitely does not state all protein synthesis is shut off, but that host protein synthesis is differentially shut down. This is very distinct from shutting off all protein synthesis, because that would stop the virus from being able to do any replication, and would necessarily cause the death of the virus because as soon as it infected a cell, the cell, and the virus, would die.

Applicant argues that the VHS shutoff protein is not obviated (p. 11, paragraph 1).

Such is not persuasive. The rejection clearly addresses this aspect.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633